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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/710,633	11/08/2000	Stephen B.H. Kent	TSRI 478.0C1	6210

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08/28/2002

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EXAMINER

RUSSEL, JEFFREY E

ART UNIT

PAPER NUMBER

1653

DATE MAILED: 08/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/710,633

Applicant(s)

KENT ET AL.

Examiner

Jeffrey E. Russel

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 July 2002 .
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 8,10-14,24,26 and 29-31 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 8,10-14,24,26 and 29-31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 July 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ .
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_ .
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_ .

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1. The Sequence Listing filed August 6, 2001 is approved.
2. The amendment instruction in the last two lines of Applicants' response filed July 1, 2002 gives incorrect page and line numbers. The paragraph starting on page 16, line 3, and extending to page 16, line 10, was substituted with the paragraph at the top of page 7 of Applicants' response.
3. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

The serial number of the parent non-provisional application is incorrect. Also, the filing date of this application should be included in the claim for priority.

Correction is required.

4. The disclosure is objected to because of the following informalities: The Schemes set forth in the specification constitute flowcharts and/or figures, and need to be deleted from the specification and re-submitted as proposed new drawings. See 37 CFR 1.58(a). At page 9, line 24, one of the two occurrences of "the" should be deleted. Appropriate correction is required.

Applicants' response did not contain any actual amendment instructions deleting the Schemes/flowcharts from the specification. Applicants also did not respond to the objection to page 9, line 24, of the specification.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

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6. Claims 11-14, 24, 26, and 29-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no original disclosure of derivatives of naturally isolatable proteins containing one or more cysteine residues that are not found in the naturally isolatable protein (see claims 11 and 24). The original disclosure does not include the concept of altering a naturally-occurring protein's amino acid sequence by replacing amino acids with cysteine residues or by inserting cysteine residues into the amino acid sequence so that a derivative of the naturally-occurring protein can be synthesized by the disclosed method.

7. Claims 29-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 29 is dependent upon canceled claims 27 and 28.

8. Claims 8, 10, and 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 96/34878 (which issued based upon Applicants' priority document PCT/US95/05668). The WO Patent Application '878 teaches Applicants' claimed invention. This rejection will be withdrawn once Applicants have inserted the appropriate claim for priority into the specification (see paragraph 3 above).

9. Claims 8, 10, and 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by the Dawson et al article. The Dawson et al article teaches ligating two oligopeptides, one oligopeptide having a C-terminal thioester and the other oligopeptide having an N-terminal cysteine residue, in the presence of a thiol. Spontaneous rearrangement results in the formation

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of an amide bond. The oligopeptides are prepared by solid phase synthesis and conversion of the C-terminal thiol. See, e.g., page 777, column 1 and Figure 1, and page 778, footnote 2. This rejection will be withdrawn once Applicants have inserted the appropriate claim for priority into the specification (see paragraph 3 above).

10. Claims 24, 26, and 29-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Yamagishi et al (U.S. Patent No. 4,990,455). Yamagishi et al teach human TNF in which residue 145 is replaced with cysteine. Residue 144 is glutamic acid, a non- $\beta$ -branched amino acid residue. Note that process steps do not impart patentability to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art.

11. Applicant's arguments filed July 1, 2002 have been fully considered but they are not persuasive.

The terminal disclaimer filed July 1, 2002 has been approved and overcomes the obviousness-type double patenting rejection set forth in the previous Office action.

The rejection under 35 U.S.C. 112, first paragraph, concerning the insertion of cysteine residues into naturally isolatable proteins is maintained. The issue is not what a chemist of ordinary skill would readily appreciate, but rather is whether or not the inventor had possession of the claimed invention at the time the application was filed. This conclusion is possible only if the specification clearly conveys the information that an Applicant has invented the subject matter which is claimed. In general, see MPEP 2163. As noted in the rejection, the concept of replacing amino acids with cysteine residues or inserting cysteine residues into a naturally isolatable protein is not found in the specification. There are no examples in the specification where this substitution or insertion is performed - the fragments which are to be ligated in the

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Examples are defined only by the location of the cysteine residues in the naturally isolatable protein which is to be synthesized. The mere recitation of a desired goal in the specification, e.g., the prospect of unrestricted variation of protein covalent structure, without discussion of the means to achieve it, does not constitute a full, clear, concise and exact description to the claim limitations in question.

The rejection over the Clark-Lewis et al article set forth in the previous Office action is withdrawn in view of the new claim limitation requiring the presence of a cysteine which is not found in the naturally isolatable protein.

The rejection over Shaw et al set forth in the previous Office action is withdrawn in view of the new claim limitation requiring that there be at least 30 amino acid residues attached to the N-terminus of the non-naturally occurring cysteine residue.

The rejection over Bell et al (see especially Figure 1) set forth in the previous Office action is withdrawn in view of the new claim limitations requiring that there be at least 30 amino acid residues attached to the N-terminus of the non-naturally occurring cysteine residue and requiring that the amino acid residue attached to the N-terminus of the non-naturally occurring cysteine residue be non- $\beta$ -branched. Threonine, which occurs at residue 100 of human IFN- $\beta$ , is  $\beta$ -branched.

The rejection over the Abrahmsen et al article set forth in the previous Office action is withdrawn in view of the new claim limitation requiring that the amino acid residue attached to the N-terminus of the non-naturally occurring cysteine residue be non- $\beta$ -branched. Threonine, which occurs at residue 220 of subtilisin BPN' *Bacillus amyloliquefaciens*, is  $\beta$ -branched.

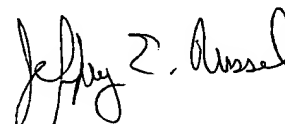
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12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Christopher Low can be reached at (703) 308-2923. The fax number for Art Unit 1653 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 305-7401 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel  
Primary Patent Examiner  
Art Unit 1653

JRussel  
8/26/02